

# The Invasive Investigator

Newsletter for the DoD Invasive Streptococcus Surveillance

## First Cases of Invasive *S. pyogenes* Infection Reported

### Introduction

We continue to conduct surveillance at high-risk military training facilities throughout the United States. These sites and their points of contact are listed on page 2 of this newsletter. We can apply this protocol to investigate cases of invasive streptococcal infection among active-duty personnel occurring at other sites. For more information regarding the protocol, please contact CDR Gray (Navy), MAJ Mahmoud (Army) or MAJ Gibson (Air Force).

### News and Notes

This is the second newsletter for the protocol "An Epidemiological Study of Invasive *Streptococcus pyogenes* Infection Among U.S. Military Personnel." We hope that this newsletter will provide a better understanding of study progress and findings. Any changes to the protocol will be addressed in this and subsequent newsletters.

First, we would like to thank everyone involved for their excellent work in maintaining the surveillance data. Nearly all of the participating training centers have provided complete and timely information (See table, page 3). We realize you are busy with your regular duties, and we greatly appreciate your efforts on behalf of this study.

Two cases of invasive *S. pyogenes* infection have been reported since the study began, both of which occurred at the Naval Training Center in Great Lakes, Illinois. Both cases were identified via positive wound cultures; neither case had a positive blood culture. The first case was a male recruit who had a positive culture from a facial wound. As per protocol, close contacts of the patient had throat cultures performed, 6 of which were also positive. Acute and convalescent (4 weeks later) sera specimens were obtained on the patient and on the 6 positive close

contacts. Subsequent analysis found that all 7 of the isolates were of the same *S. pyogenes* subtype. This was communicated to the preventive medicine officer at Great Lakes, along with other test results, including minimum inhibitory concentrations (MICs) of the isolates to 5 different antibiotics, toxin gene typing, and acute and convalescent ASO and DNaseB titers (See table, page 4). The second case had a positive culture from a leg wound; however, he had finished recruit training, and we were unable to study him further. Several close contacts of this patient had throat cultures performed and all were negative.

These cases present two important things to bear in mind with respect to this study:

1. A patient does not need to have a positive blood culture to qualify as a case. Invasive *S. pyogenes* infection is defined as the isolation of Group A Streptococcus from any normally sterile site, including blood, surgical wound, tissue biopsy, and cerebrospinal, pleural, or peritoneal fluid. Additionally, a patient is considered as a probable case (for the purposes of this study) when he/she has a positive *S. pyogenes* culture from a nonsterile site (throat, sputum, vagina, superficial skin lesion) along with toxic shock syndrome (TSS). Please refer to the case definition on page 5 for further details.

2. We can provide supplementary test results that may help you in making clinical decisions.

Besides surveillance, one of the primary goals of this study is to determine why *S. pyogenes* becomes invasive in some people and not in others. To accomplish this, we need a large amount of data. That's why it is very important all training centers remain vigilant

for patients who meet our case definition as outlined on page 5. We're counting on you to help make this study a success!

### Protocol Modification

Nothing teaches like experience. As we went through the protocol during the course of the first case of invasive strep, we found a couple of errors or omissions in the flow diagram in the protocol. We have included a revised flow diagram in this newsletter (page 6). Please refer to this to help determine the steps you should take when a case of invasive strep is identified. This new flow diagram should be easier to follow than the previous one.

### Reminder

Once a case of invasive disease has been identified and local medical authorities and investigators decide an investigation is appropriate, the Naval Health Research Center's Emerging Illness Team may be able to supplement local preventive medicine assets by deploying an assist team. If you have a suspected case of invasive *S. pyogenes* infection, please contact us and we'll be happy to assist you in implementing the study protocol.

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## Tests of Streptococcal Isolates

Study Number	Patient or Contact	M & T Type	[----- Toxin genes -----] [-----]			-----Minimum Inhibitory Concentrations -----						
			Strep Group	SpeA	SpeC	SpeF	SSA	Azithromycin	Cephalexin	Clindamycin	Erythromycin	Penicillin
001-1	Patient	M1T1	A	Y	N	Y	N	2	0.125	0.25	0.25	0.016
001-2	Contact	M1T1	A	Y	N	Y	N	2	0.19	0.25	0.38	0.023
001-2*	Contact	M1T1	A	Y	N	Y	N	6	0.38	0.25	0.50	0.064
001-3	Contact	M1T1	A	Y	N	Y	N	2	0.19	0.25	0.25	0.016
001-4	Contact	M1T1	A	Y	N	Y	N	2	0.19	0.25	0.25	0.023
001-5	Contact	M1T1	A	Y	N	Y	N	2	0.125	0.25	0.19	0.016
001-6	Contact	M1T1	A	Y	N	Y	N	2	0.125	0.38	0.19	0.032
001-7	Contact	M1T1	A	Y	N	Y	N	2	0.25	0.38	0.38	0.016

\* Second GAS isolate was cultured from this person after 3 week convalescent period

## Serology Testing

## Percent Inhibition of Mitogenicity

Study Number	[-----] [-----] [-----] 1 % Plasma			[-----] [-----] [-----] 5 % Plasma			[-----] [-----] [-----] 5 % Plasma			[-----] [-----] [-----] 5 % Plasma		
	SpeA	SpeB	SpeC	Supernatant	SpeA	SpeB	SpeC	Supernatant	PHA	Acute ASO	Convales. ASO	Acute DNase B
001-1	0	21	0	76	0	42	6	96	0	120	160	60
001-2	0	0	0	26	16	46	11	12	13	480	400	400
001-3	53	0	0	92	100	46	0	100	51	160	160	480
001-4	24	0	0	8	71	0	0	37	41	160	800	80
001-5	52	0	0	44	98	10	2	47	17	240	640	120
001-7	0	57	38	30	6	91	83	57	64	320	400	480

Note: Subject number 001-6 did not provide blood samples.

## Interpretations:

## Strep Isolates:

- The M, T, and toxin typing indicate that all of the strep isolates are of the same subtype.
- The MICs show that this strain of *S. pyogenes* was susceptible to all of the antibiotics tested.

## Serology:

- The percent inhibition of mitogenicity tests indicates how well an individual's antibodies inhibit the toxicity of various agents. The most informative result is how much the plasma inhibits (or neutralizes) the toxicity of the supernatant from the strep isolate. There was a wide range of neutralizing activity among the subjects, and the patient's neutralizing activity was surprisingly high. This may have been because the patient's blood sample was drawn a week after onset of symptoms and he may have developed an immune response during this time.
- The ASO and DNaseB titers remained unchanged in the patient, however, they showed a response in 2 of the 5 close contacts.

**Case Definitions:**  
**Invasive *Streptococcus pyogenes* Infection and**  
**Streptococcal Toxic Shock Syndrome (STSS)**

**Invasive *S. pyogenes* infection:** The isolation of *S. pyogenes* from a normally sterile site, such as blood, surgical wound, tissue biopsy, and cerebrospinal, pleural, or peritoneal fluid.

**Streptococcal Toxic Shock Syndrome:**<sup>1</sup>

**A. Definite case:**

1. Isolation of *S. pyogenes* from a normally sterile site as listed above
2. Hypotension - SBP  $\leq 90$  mmHg
3. Two or more of the following:
  - a. Renal impairment - creatinine  $\geq 177$  mol/L ( $\geq 2$  mg/dL)
  - b. Coagulopathy - platelets  $\leq 100 \times 10^9/L$  ( $\leq 100,000/mm^3$ )
  - c. Liver abnormalities - SGOT, SGPT, or total bilirubin  $\geq 2$  times the upper limit of normal
  - d. Adult Respiratory Distress Syndrome (ARDS)
  - e. A generalized erythematous macular rash that may desquamate
  - f. Soft tissue necrosis, including necrotizing fasciitis or myositis, or gangrene

**B. Probable case:**

1. Isolation of *S. pyogenes* from a nonsterile site (throat, sputum, vagina, superficial skin lesion)
2. Hypotension - SBP  $\leq 90$  mmHg
3. Two or more of the following:
  - a. Renal impairment - creatinine  $\geq 177$  mol/L ( $\geq 2$  mg/dL)
  - b. Coagulopathy - platelets  $\leq 100 \times 10^9/L$  ( $\leq 100,000/mm^3$ )
  - c. Liver abnormalities - SGOT, SGPT, or total bilirubin  $\geq 2$  times the upper limit of normal
  - d. Adult Respiratory Distress Syndrome (ARDS)
  - e. A generalized erythematous macular rash that may desquamate
  - f. Soft tissue necrosis, including necrotizing fasciitis or myositis, or gangrene

<sup>1</sup>Adapted from Stevens DL. Streptococcal toxic-shock syndrome: spectrum of disease, pathogenesis, and new concepts in treatment. *Emerging Infectious Diseases*. 1995;1(3): 69-77.